

Remarks

The Examiner rejected claim 31 under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent Application Publication No. 2002/0098185 to Sims et al. ("Sims"), and further in view of U.S. Patent No. 7,005,523 to Dombroski et al. ("Dombroski"). The Examiner has acknowledged that "Sims does not explicitly mention that said combination comprises anakinra and IL-18BP, or that IL-1Ra is anakinra" (page 4, last sentence before the first full par. of the 5/20/09 OA). However, the Examiner continues to argue that "Sims teaches general combination of IL-18 antagonists with IL-1 antagonist" (par. 3, page 3, 1/21/10 Office Action), and that both these classes of compounds were known, for example for the treatment of rheumatoid arthritis (RA) and therefore a combination of the specific IL-18BP and anakinra as claimed would be obvious.

The examiner rejected Applicants' previous submission of evidence that prior art specifically teaches that **anakinra should not be combined with many of the compounds used to treat arthritis and listed in Dombroski as well as Sims**. Specifically, the evidence in question stated that "**Kineret should not be used** with medicines called Tumor Necrosis Factor (TNF blocking agents) such as ENBREL® (etanercept), Humira™ (adalimumab), or Remicade® (infliximab)." The Examiner alleged that the argument is irrelevant because it does not directly discuss the combination of IL-18BP and anakinra (Kineret).

Applicants respectfully disagree and submit that the rejection should be withdrawn for the following reasons.

Applicants submit that a skilled artisan was well aware that TNF and IL-18 are intricately linked and that TNF blockers also block IL-18.

For example, Applicants submit herewith an article by Puren et al. (J. Clin. Invest, 1998, Exhibit A), that specifically shows that TNF-BP (TNF binding protein, i.e. a TNF blocker) also inhibits IL-18 induction (see, e.g., Fig. 9). Thus, contrary to the Examiner's assertion, a skilled artisan, at the time of filing the present application was aware that **compounds that block TNF also block IL-18** as evidenced by Exhibit A.

As set forth in Exhibit I, the prior art taught that TNF blockers should not be combined with Kineret (anakinra). Knowing that TNF blockers also block IL-18, it is evident to a skilled artisan, that the warnings of simultaneous use of Kineret (anakinra) regarding combination with TNF-blockers also apply to IL-18 blockers, such as IL-18BP.

In other words, the prior art teaching that one should not combine Kineret (anakinra) with TNF blocking agents also teaches that one should not combine Kineret (anakinra) with IL-18 blocking agents, such as IL-18BP.

Accordingly, the prior art teaches directly against the present invention of a combination of anakinra and IL-18BP.

In view of the additional evidence in the form of Exhibit A, and arguments set forth, *supra*, Applicants respectfully request that the rejection of claim 31 under 35 U.S.C. 103(a) as allegedly being unpatentable over Sims, and further in view of Dombroski, should be withdrawn.

In view of the foregoing, Applicants respectfully submit that claim 31 is now in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the Commissioner is hereby is authorized to charge our deposit account No. 50-0850. Any overpayments should also be deposited to said account.

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Customer No.: 50828

Respectfully submitted,

/Leena H. Karttunen/

David S. Resnick (Reg. No. 34,235)
Leena H. Karttunen (Reg. No. 60,335)
Nixon Peabody LLP
(617) 345-6057 / 1367